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MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C.			CLOW, LORI A	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/547,944	FRIMURER ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	LORI A. CLOW	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 06 January 2011.

2a) This action is **FINAL**.                            2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-45 is/are pending in the application.

4a) Of the above claim(s) 7-16,32-34,36 and 38-43 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-6,17-31,35,37,44 and 45 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on 06 September 2005 and 06 January 2011 is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 1/6/2011.

4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.

5) Notice of Informal Patent Application

6) Other: \_\_\_\_\_.

### **DETAILED ACTION**

Applicants' response, filed 6 January 2011, has been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-45 are currently pending.

Claims 7-16, 32-34, 36, and 38-43 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species or invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 15 April 2010.

Claims 1-6, 17-31, 35, 37, 44, and 45 are examined herein.

It is noted that claims 14-16 are now withdrawn claims, as they have been amended to depend from claim 7, a non-elected invention.

### **Oath**

This objection is re-iterated from the previous Office Action. Applicant has not corrected the Oath as of the date of this Office Action.

It appears as if Applicant intends to claim Foreign Priority to Danish Application PA 2003 00353, filed 4 March 2003. However, the Oath indicates, on the first page, that "no such foreign applications have been filed" (see checked box). Perhaps this is a typographical error. If so, please correct by re-submitting a new Oath.

**Priority**

This remark is re-iterated from the previous Office Action.

As indicated above, it appears as if Applicant intends to claim Foreign Priority based on an application filed in Denmark on 7 March 2003. It is noted, however, that applicant has not filed a certified copy of the foreign application as required by 35 U.S.C. 119(b).

Until such time as the Oath is corrected and certified copies are received, the priority date accorded the instant Application is 5 March 2004 (the date of the PCT).

**Drawings**

The Replacement Drawing for Figure 1 submitted in the response of 6 January 2011 is accepted. The Drawings submitted 6 September 2005 are accepted.

**Specification**

The objections to the Specification are hereby withdrawn in view of the submitted amendments.

**Sequence Compliance**

The Sequence listing and CRF submitted in the response of 6 January 2011 has been entered and is accepted.

**Information Disclosure Statement**

The Information Disclosure Statement filed 6 January 2011 has been considered. A signed copy of PTO Form 1449 is included with this Office Action.

**Claim Rejections - 35 USC § 112**

The outstanding rejections under 35 USC 112, 2<sup>nd</sup> paragraph have been withdrawn in view of the claim amendments.

**Claim Rejections - 35 USC § 101-Non-statutory Subject Matter**

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6, 17-31, 35, 37, 44 and 45 remain rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Newly recited portions of the below rejection are necessitated by claim amendment.

Claims 1-6, 17-31, 35, 37, and 44 are drawn to a pseudo-sequence method for identifying similarities in binding sites of a first 7TM receptor with those of one or more further 7TM receptors by comparing physicochemical properties of selected amino acid residues.

Based upon consideration of all of the relevant factors with respect to the claim as a whole, the instant claims are held to claim an abstract idea, and are therefore rejected as ineligible subject matter under 35 U.S.C. 101. The rationale for this finding is explained below:

Making reference to the Interim Guidance for Determining Subject Matter Eligibility for Process Claims in View of Bilski v. Kappos (75 FR 43922 at 43927 (27 July 2010)), factors that weigh against the eligibility of a process claim include no express or inherent recitation of a machine or transformation. Further, weighing against eligibility is a claim that is merely a statement of a general concept, such that it includes, for example, mathematical concepts such as algorithms, spatial relationships, geometry, etc...

In the instant case, claims 1-6, 14-31, 35, 37, and 44 are not patent eligible under the Interim Guidance because the claims merely recite mathematical concepts of manipulating data by using a pseudo-sequence to assign physicochemical descriptors to amino acid residues and generate a similarity score by comparing the physicochemical descriptors without the recitation of a specific machine in which to perform such steps or without the recitation of an actual transformation of the data to a different state or thing. The claims represent “abstract” ideas, in that there are no limitations as to the mechanism for performing such steps. As such, the claims are non-statutory.

Claim 45 is drawn to a “computer readable medium carrying a computer program”. A computer-readable medium reads on carrier waves, which read on transitory propagating signals which are not proper patentable subject matter because they do not fit within any of the four statutory categories of invention (In re Nijten, Federal Circuit, 2006). The Specification does not define which type of medium, transitory or non-transitory, are intended and as such, the Specification includes both transitory and non-transitory embodiments and the claims are not statutory.

Applicant is referred to OG Notice for Subject Matter Eligibility of Computer Readable Media (<http://www.uspto.gov/web/offices/com/sol/og/2010/week08/TOC.htm#ref20>), which states the following:

The USPTO recognizes that applicants may have claims directed to computer readable media that cover signals per se, which the USPTO must reject under 35 U.S.C. § 101 as covering both non-statutory subject matter and statutory subject matter. In an effort to assist the patent community in overcoming a rejection or potential rejection under 35 U.S.C. § 101 in this situation, the USPTO suggests the following approach. A claim drawn to such a computer readable medium that covers both transitory and non-transitory embodiments may be amended to narrow the claim to cover only statutory embodiments to avoid a rejection under 35 U.S.C. § 101 by adding the limitation "non-transitory" to the claim. Cf. *Animals - Patentability*, 1077 Off. Gaz. Pat. Office 24 (April 21, 1987) (suggesting that applicants add the limitation "non-human" to a claim covering a multi-cellular organism to avoid a rejection under 35 U.S.C. § 101). Such an amendment would typically not raise the issue of new matter, even when the specification is silent because the broadest reasonable interpretation relies on the ordinary and customary meaning that includes signals per se.

### ***Response to Applicant's Arguments***

1. Applicant argues that "the Examiner erroneously relied on the machine-or-transformation test as the sole test under 35 USC 101" and that "the Supreme Court in *Bilski* emphasized the broad scope of patent eligible subject matter evidenced by the text of 35 USC 101 ("any new and useful process, machine, manufacture, or composition of matter, or any useful improvement thereof") and the intent of Congress that the patent laws be given a wide scope. *Id.*, at 3225." Applicant further contends that although the claimed methods use mathematical formulas and algorithms, this does not render the methods so abstract as to take them outside of the broad category of patent-eligible processes" and that "the Federal Circuit recognized that algorithms and formulas, even when constituting a significant part of the claimed process, do not necessarily result in the loss of patent eligibility (citing *Research Corp. v.*

Microsoft (Fed. Cir. 2010) Slip Op. at 15)." As such, Applicants submit that the claimed methods fall within the broad statutory category of patent eligible processes.

This is not persuasive. It is first noted that the Interim Guidance for Determining Subject Matter Eligibility for Process Claims in View of Bilski v. Kappos (75 FR 43922 at 43927 (27 July 2010)) as a result of the Supreme Court Decision in Bilski, was not published until 27 July 2010 and that the Examiner correctly assessed the claimed subject matter with regard to the Federal Circuit decision in In re Bilski (In re Bilski, 545 F.3d 943, 88 USPQ2d 1385 (Federal Circuit, 2008) that was the precedence as of the Office Action of 6 June 2010.

That notwithstanding, the Supreme Court stated that the machine-or-transformation test is a "useful and important clue" and an "investigative tool" for determining whether some claimed methods are statutory processes but "is not the sole test for deciding whether an invention is a patent-eligible process" Slip op. at 8. Following the Supreme Court decision and the Interim Guidance, in which Bilski reaffirms Diehr, the Examiner contends that the instant claims are drawn to abstract ideas (mathematical manipulations) and that there is not a sufficient application of the abstract idea to a known structure or process" (from Diamond v. Diehr, 450 U.S. 175, 187 (1981)). The factors that weigh against patent eligibility herein are recited above and re-iterated herein: no express or inherent recitation of a machine or transformation and recitation of a claim that is merely a statement of a general concept, such that it includes, for example, mathematical concepts such as algorithms, spatial relationships, geometry, etc...

2. Applicant further argues that the claims meet the transformation arm of the machine-or-transformation test because "the active step of generating a similarity score to quantify how similar the binding sites of the 7TM receptors are, as required by claims 1-6, 14-31, 35, and 37,

transforms the pseudo-sequences of multiple 7TM receptors in to a plurality of similarity scores which provide a comparison between binding sites of the multiple 7TM receptors".

This is not persuasive. The steps of the method recite generating similarity scores by merely comparing data (the descriptors of one receptor to the descriptors of another etc...).

Applicant has not shown that an actual transformation has taken place. Further, simple mathematical functions are not transformation of data to a different state. One could perform said method by simply looking at a chart or a spread sheet, so what actual transformation has taken place?

In light of the above, the claims remain rejected as being directed to non-statutory subject matter.

### **Claim Rejections - 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 17-31, 37, 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lapinsh et al. (Protein Science (2002) Vol. 11; 795-805; previously cited) in further view of Lapinsh et al. (Biochimica and Biophysica Acta (2001) Vol. 1525, pages 180-190; hereinafter Lapinsh (2)). This is a new grounds of rejection as necessitated by claim amendment.

The instant claims are drawn to a method for identifying similarities in binding sites of a first 7TM receptor with those of one or more further 7TM receptors by generating a similarity score as defined by comparing the physicochemical descriptors of 7TM receptors.

In regard to claims 1, 44, and 45, Lapinsh et al. teach a method wherein classification of G-protein coupled receptors is attained according to the principal chemical properties of their amino acid sequences. Primary amino acid sequences are translated into vectors based on the principal physicochemical properties of the amino acids and transformation of the data into a uniform matrix is applied (abstract). Lapinsh is distinguishing families of GPCR, therefore inherently identifying similarities (as well as differences) in binding sites.

In regard to claims 2 and 4, the comparison is made without data related to binding affinity (page 796, column 1 and 2).

In regard to claim 3, Lapinsh et al. teach using physicochemical properties (p. 802, column 2).

In regard to claim 17, the method may be computer implemented (page 796, column 1).

In regard to claim 21 and 22, Lapinsh et al. teach using transmembrane parts of the GPCRs (which contain extracellular loops) (page 797, column 1).

In regard to claim 23, Lapinsh et al. teach physicochemical descriptors with interaction features (page 796, column 2).

In regard to claim 24, Lapinsh et al. teach hydrophobicity, for example, at page 796, column 2).

In regard to claim 25, Lapinsh et al. teach three-dimensional features (Figure 1).

In regard to claim 26, Lapinsh et al. teach PCA (page 797, column 2).

In regard to claims 27-29, Lapinsh et al. teach various physicochemical descriptors at page 797, column 2.

In regard to claim 37, Lapinsh et al. teach ranking (Table 2).

Lapinsh et al. do not specifically teach using a pseudo-sequence, as is now claimed, however Lapinsh (2) teaches using portions of various amino acid sequences that correspond to various positions within TM1-TM7, such as TM1 29-45, TM2 70-86, TM3 100-122, TM4 145-159, TM5 183-199, TM6 280-292, and TM7 310-321. The instant Specification defines an amino acid pseudo-sequence to be selected amino acid residues in sequential or non-sequential

order, involved in one or more ligand binding sites in 7TM receptors. Therefore, Lapinsh (2) teaches this embodiment of the instant claim.

Lapinsh et al. do not specifically teach the embodiments of claims 5, 6, 18-20, 30, 31, and 44, however, Lapinsh (2) teaches that various numbers of amino acid residues may be used (claims 5 and 6) (Lapinsh (2) at page 181. Lapinsh (2) further teaches that models are used (the proteo-chemometric model (page 181; claim 18). Lapinsh (2) teaches that adrenoreceptors are used, therefore meeting the limitation of claim 19 (page 181). Lapinsh (2) teaches using TM1-TM7 for alignment, which inherently contain  $\alpha$ -helices (page 181; claim 20). Lapinsh (2) teaches using principal components in the descriptor analysis (page 181; claim 30 and 31).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have combined the alignment and similarity features of Lapinsh et al. with the proteo-chemometric model of Lapinsh (2) so as to better assess GPCRs. One of skill in the art would have had an expectation of success in doing so because Lapinsh et al. teach that in alignment of TMs, there is a wide variation and functional units vary, sometime substantially (page 797), therefore by aligning TMs using certain positions, as is taught by Lapinsh (2), a more accurate approximation can be made and then z-scales applied (page 181, column 2).

**2.** Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lapinsh et al. (Protein Science (2002) Vol. 11; 795-805; previously cited) in further view of Lapinsh et al. (Biochimica and Biophysica Acta (2001) Vol. 1525, pages 180-190; hereinafter Lapinsh (2)), as applied to claims 1, 17, and 28 above, in further view of Brown et al. (Journal of Chem. Inf.

Comput. Sci. (1997) Vol. 37, pages 1-9). This is a new grounds of rejection as necessitated by claim amendment.

The instant claims are drawn to a method for identifying similarities in binding sites of a first 7TM receptor with those of one or more further 7TM receptors by generating a similarity score as defined by comparing the physicochemical descriptors of 7TM receptors.

In regard to claim 1 Lapinsh et al. teach a method wherein classification of G-protein coupled receptors is attained according to the principal chemical properties of their amino acid sequences. Primary amino acid sequences are translated into vectors based on the principal physicochemical properties of the amino acids and transformation of the data into a uniform matrix is applied (abstract). Lapinsh is distinguishing families of GPCR, therefore inherently identifying similarities (as well as differences) in binding sites. In regard to claim 17, the method may be computer implemented (page 796, column 1). In regard to claims 28, Lapinsh et al. teach various physicochemical descriptors at page 797, column 2.

Lapinsh et al. do not specifically teach using a pseudo-sequence, as is now claimed, however Lapinsh (2) teaches using portions of various amino acid sequences that correspond to various positions within TM1-TM7, such as TM1 29-45, TM2 70-86, TM3 100-122, TM4 145-159, TM5 183-199, TM6 280-292, and TM7 310-321. The instant Specification defines an amino acid pseudo-sequence to be selected amino acid residues in sequential or non-sequential order, involved in one or more ligand binding sites in 7TM receptors. Therefore, Lapinsh (2) teaches this embodiment of the instant claim.

Neither Lapinsh et al. nor Lapinsh (2) specifically teach using the Tanimoto Similarity Measure as in claim 35, however, Brown et al. teach a method for detecting the ability to

accurately predict values for physical properties of a structure related to various interactions, from a known value (descriptor value) for other structures which are shown to be structurally similar to the first by the descriptor in question (abstract). Brown et al. disclose using similarity measurements, such as using the Tanimoto similarity measure (page 2, column 2 to page 3, column 2).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have combined the alignment and similarity features of Lapinsh et al. with the proteo-chemometric model of Lapinsh (2) so as to better assess GPCRs. One of skill in the art would have had an expectation of success in doing so because Lapinsh et al. teach that in alignment of TMs, there is a wide variation and functional units vary, sometime substantially (page 797), therefore by aligning TMs using certain positions, as is taught by Lapinsh (2), a more accurate approximation can be made and then z-scales applied (page 181, column 2). It would have further been prima facie obvious to include similarity measurements using the Tanimoto measure because it was well known in the art at the time of the invention to use such analysis when comparing receptors or identifying similarities between receptors, as is demonstrated by , Brown et al. for assessing binding.

## Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### **Inquiries**

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is

(866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

March 10, 2011  
/Lori A. Clow, Ph.D./  
Primary Patent Examiner  
Art Unit 1631